

## REMARKS

Applicant wishes to thank Examiner Kim and SPE Bragdon for the careful consideration given to this application, as well as the courteous telephonic interview extended to the undersigned on December 7, 2006. During the interview, claim amendments incorporating acceptable language were discussed. Examiner Kim and SPE Bragdon provided the undersigned with a copy of "ANNEX 3: Comments of the USPTO, Trilateral Project WM4" which was used in the preparation of Claims 21-23 and 53-62 presented herein. Claims 1-23 and 26-62 are pending. Claims 1-19 and 26-52 stand withdrawn. Claims 24 and 25 have been cancelled. Claims 53-62 are new. Support for all amended and new claims can be found in the specification as originally filed. No new matter has been added.

### Election

In order to be fully responsive to the Office Action, Applicant affirms the election, with traverse, of the invention of Group II (Claims 20-25).

### Priority

The Examiner alleges that U.S. Provisional Application No. 60/443,590 filed January 30, 2003 does not support the present application (U.S. Application No. 10/769,218). Applicant respectfully disagrees.

The disclosure of U.S. Provisional Application No. 60/443,590 includes all of the data submitted in the present application as filed, including detailed descriptions of the proteins and peptides used, methods used to prepare these proteins and peptides, descriptions of crystallographic data obtained and methods for obtaining the crystallographic data, description of critical interactions between inhibitory molecules or peptides and an initiator caspase, and all of the figures used in support of this data. Moreover, the Examiner has used the published version of U.S. Provisional Application No. 60/443,590 (Molecular Cell, 2003, Vol. 11, p. 519-527 by Shiozaki et al.) in a rejection under 35 U.S.C. § 102(b) as evidence that the claimed interactions between an inhibitory molecule and an initiator caspase occur. Accordingly, Applicant submits that U.S. Provisional Application No. 60/443,590 provides sufficient support for amended claims 20-23 and new claims 53-62. Applicant respectfully requests that the claimed benefit of priority

to U.S. Provisional Application 60/443,590 be acknowledged and the present application be given a priority date of January 31, 2003. Reconsideration is respectfully requested.

#### Objections to the Specification

The specification stands objected to as containing the following informalities: the Examiner has objected to the title as not being descriptive of the claims; the Examiner has objected to the Abstract as not completely describing the disclosed subject matter; the Examiner alleges that the catalytic subunit of caspase-9 contains residues 140-416 and not residues 139-416 as indicated in the specification as filed; and the Examiner alleges that the BIR3 Domain of XIAP contains residues 253-350 and not residues 252-350 as indicated in the specification as filed. Applicant has attended to all of the above identified objections to the specification. Withdrawal of the Examiner's objections is respectfully requested.

The Examiner also alleges that the application incorrectly discloses and claims priority to U.S. Provisional Application 60/443,950. Applicant respectfully disagrees. As filed, the present application claims priority to "U.S. Provisional Application No. 60/443,590 filed January 30, 2003" (see page 1, para 0001). The filing receipt mailed June 14, 2004 incorrectly identified the claimed priority document as U.S. Provisional Application No. 60/443,950 as evidenced by the filing receipt for U.S. Provisional Application No. 60/443,590 attached hereto. The claim of priority has been amended to fix typographical errors including correcting the filing date of the U.S. Provisional Application No. 60/443,590. Therefore, the claim of priority is correctly set forth in the present application. Applicant has concurrently filed herewith a request to correct the filing receipt to reflect the proper priority document (i.e. U.S. Provisional Application No. 60/433,590) as well as a new Application Data sheet. Withdrawal of the Examiner's objection is respectfully requested.

#### Rejections under 35 U.S.C. § 112

Claims 20-25 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The Examiner alleges that it is unclear whether the claimed polypeptide requires only the four identified amino acid residues or a polypeptide having a surface groove defined by these amino acid residues in an orientation required by the three-dimensional structure coordinate data.

Applicant has amended independent claim 20 to clarify that the compound has a structure and function of Pro325, Gly326, His343, and Leu344 of XIAP BIR3, which corresponds to a region of XIAP BIR 3 that interacts with caspase-9 as identified by crystallographic data presented in the specification. Accordingly, Applicant requests that this rejection be withdrawn.

Claims 20-25 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The Examiner alleges that the parentheses in claims 20 and 24-25 make it unclear whether all of the amino acids in the SEQ ID NO must be included.

Applicant has removed the SEQ ID NO's and all parentheses from claims 20 and 24-25, and independent claim 20 has been amended to clarify that the compound has the structure and function of Pro325, Gly326, His343, and Leu344 of XIAP BIR3, thereby attending to the Examiner's rejection. Accordingly, Applicant requests that this rejection be withdrawn.

Claim 24 stands rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Claim 24 has been cancelled, rendering the Examiner's rejection moot.

Claims 20-25 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification. The Examiner alleges that the claims are directed to any polypeptide having di-peptides of Pro Gly and His Leu and that the specification cannot describe the structure of a very broad claimed genus, nor would one skilled in the art be in possession of the claimed genus polypeptides. Additionally, claims 20-25 stand rejected under 35 U.S.C. § 112, first paragraph as not providing enablement for a method of inhibiting an initiator caspase with any polypeptide including the claimed four amino acid residues. The Examiner alleges that the specification fails to describe how to make and use the claimed genus polypeptide sufficiently in the claimed method, and therefore, it would require undue experimentation for a method of using the claimed genus polypeptide.

Applicant has amended independent claim 20 to clarify that the inhibitor has the structure and function of Pro325, Gly326, His343, and Leu344 of XIAP BIR3. Support for this amendment can be found throughout the specification. In particular, the interactions of these specific amino acids to the binding cleft of caspase-9 are described in paragraphs [0034] to [0036] of the specification as originally filed and can be visualized in Fig. 3; methods for testing the binding between an inhibitory molecule and an initiator caspase are described in paragraphs [0039] to [0040] of the specification as originally filed and examples provided in Examples 3

and 4 (paragraphs [0080] to [0084]); preparation of inhibitory molecules, initiator caspases, and complexes of an inhibitory molecule and an initiator caspase is described in Example 1 (paragraph [0077]); a detailed description of protein-protein interface between an exemplary inhibitory molecule and the initiator caspase is described in paragraph [0031] to [0038]; and confirmation of this analysis is provided in paragraphs [0039] to [0040] of the specification as originally filed. Accordingly, the method of amended claim 20 is fully supported by the specification as filed and would not require undue experimentation. Reconsideration and withdrawal of the Examiner's rejection is respectfully requested.

#### Rejection under 35 U.S.C. § 101

Claims 20-25 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. The Examiner alleges that the claims as written do not distinguish over the steps occurring in human cells as they naturally exist, and in the absence of the hand of man, the products are considered non-statutory.

As amended, independent claim 20 includes the step of identifying a compound and, therefore, removes any issue under 35 U.S.C. § 101. Accordingly, reconsideration and withdrawal of the Examiner's rejection is respectfully requested.

#### Rejections under 35 U.S.C. § 102

Claims 20-25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Deveraux et al. EMBO, 1999, Vol. 18, p. 5242-5251 (hereinafter "Deveraux") as evidenced by Shiozaki et al. Molecular Cell, 2003, Vol. 11, p. 519-527 (hereinafter "Shiozaki"). The Examiner alleges Deveraux teaches a method for inhibiting caspase-9 activity using a BIR3-Ring, and that the method of Deveraux would inherently form the "inhibitory complex" from co-crystal structure of Shiozaki. Applicant respectfully disagrees.

Deveraux fails to teach, suggest, or otherwise disclose a method for inhibiting activity of an initiator caspase including the step of identifying a compound having a structure and function of amino acids Pro325, Gly326, His343, and Leu344. Therefore, Deveraux fails to teach or suggest each and every step of the method of independent claim 20 and fails to anticipate amended independent claim 20.

Moreover, Deveraux teaches the inhibition of caspase-9 using a 46 amino acid peptide including both a BIR3 domain and a Ring domain and teaches against using either domain alone. Specifically, Deveraux states, “experiments involving either BIR3 or Ring domain alone suggest that neither of these is sufficient to suppress caspases by itself” (page 5249, column 1, lines 9-11). Applicant’s independent claim 20 describes critical amino acids for inhibition of caspase activity found only in the BIR3 domain XIAP, and the compounds of the current claimed invention do not require a Ring domain. Therefore, Deveraux fails to teach or suggest an inhibitor of any initiator caspase having only a BIR3 domain or any part thereof and fails to either anticipate or render obvious the current claimed invention.

With regard to Shiozaki, Shiozaki is not available as prior art under 35 U.S.C. § 102 because Shiozaki was published in February 2003, which is after the earliest claimed priority date for the present application of January 30, 2003. Moreover, the subject matter set forth in the priority document U.S. Provisional Application No. 60/443,590 is identical to Shiozaki, and is, therefore, the Applicant’s own work.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the Examiner’s rejection under 35 U.S.C. § 102(b).

## CONCLUSION

In view of the remarks presented above, it is believed that claims 20-23 and 53-62 are in condition for allowance and notice to such effect is respectfully requested. Should the Examiner have any questions regarding these remarks, the Examiner is invited to initiate a telephone conference with the undersigned.

Although Applicant believes no fees, other than the fees for the additional claims and the three (3) month petition for extension of time are due, the Commissioner is hereby authorized to charge Deposit Account No. 50-0436 for any fees that may be due in connection with this response.

Respectfully Submitted,



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